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Joana Correia Brandão

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Chronic Postoperative Pain: Impact on the Quality of Life and Recovery

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Chronic Postoperative Pain: Impact on the Quality of Life and Recovery

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Abstract and Keywords

Context: Chronic postoperative pain (CPOP) is defined as pain persisting 2 months after surgery that cannot be explained by other causes. Quality of recovery (QoR) after anaesthesia is a measure of the early postoperative health status of patients, and together with health-related quality of life (QoL) is considered a valid indicator of outcomes.

Objectives: Assess the incidence and risk factors of developing CPOP after high risk surgeries, and evaluate its impact on the quality of life and recovery.

Design: Observational, prospective study.

Setting: Post-Anaesthesia Care Unit of a tertiary hospital: Centro Hospitalar São João, Porto, Portugal.

Patients: 175 patients scheduled for elective surgery. Exclusion criteria: unable to give informed consent, cognitive impairment and urgent surgery.

Main outcome measures: The primary end point was CPOP. CPOP was assessed with the Brief Pain Inventory (BPI), QoL was evaluated with the EQ-5D EuroQol five-dimension questionnaire (EQ-5D) and QoR with the 15-item Quality of Recovery score (QoR-15). Evaluations were performed preoperatively (T0), 24 hours after surgery (T24) and 3 months after surgery (T3).

Results: 49 (28%) patients had CPOP 3 months after surgery. At T3, the problems reported by patients with CPOP were significantly larger in all EQ-5D dimensions: “mobility” ($p=0.001$), “self-care” ($p=0.001$), “usual activities” ($p<0.001$), “pain/discomfort” ($p<0.001$), and “anxiety/depression” ($p=0.002$). Patients with CPOP had lower median EuroQol Visual analogue scale (EQ VAS) (60 vs. 87, $p<0,001$). Concerning QoR-15 scores at T24, CPOP patients had lower median scores for “been able to enjoy food” ($p=0.022$), “feeling rested” ($p=0.001$), “moderate pain” ($p=0.004$), “severe pain” ($p=0.009$), “nausea or vomiting” ($p=0.049$), “feeling sad or depressed” ($p=0.013$), and for global score ($p<0.001$).

Conclusions: CPOP incidence was relevant (28%) and patients with CPOP reported worse QoR at T24 and worse QoL at T3 than those without CPOP.

Keywords: Chronic postoperative pain, quality of life, quality of recovery

Introduction

Chronic postoperative pain (CPOP) is an undervalued yet prevalent healthcare problem associated with significant morbidity and impact on physical, psycho-social, cognitive, and working domains. (1) It is defined as pain persisting 2 months after surgery that cannot be explained by other causes. (2) A neuropathic pain is often present and described as 'burning', 'shooting', or 'electric-like', and together with the presence of clinical signs of hyperalgesia or allodynia. An acute injury or surgery leads to neuroplastic changes in the peripheral and central nervous system in response to the nociceptive input. These changes cause nervous system hypersensitivity, and, if persistent, often can lead to debilitating chronic pain.

Three linked processes are implicated in the transition from acute to chronic pain and may serve as targets for prevention: i) peripheral sensitization, ii) central sensitization, and iii) descending modulation. (3) CPOP can occur with any type of surgery, but is more common following procedures with significant nerve or tissue damage. Prevalence varies greatly; the estimated prevalence for surgeries with higher risk of developing CPOP is: mastectomy 20–50%, amputation 50–85%, hysterectomy 5–30%, hernia repair 5–35%, and thoracotomy 5–65% (2). Risk factors include the type of surgery, preoperative pain, moderate-to-severe acute post-operative pain, neurotoxic radio or chemotherapy and psycho-social factors, among others (Fig. 1). (1)

Health-related Quality of Life (QoL) questions about function and perceived physical and mental health are generally considered valid indicators of service needs and intervention outcomes. (4) Recovery after surgery and anaesthesia is a complex process dependent on patient, surgical, and anaesthetic characteristics, as well as the presence of any of numerous adverse sequelae. However, it has been considered a relevant measure of the early postoperative health status of patients. Evaluating QoL and QoR may be essential for better outcomes studies in both surgery and anaesthesia. (5)

The aim of our study was to assess the incidence and risk factors of developing CPOP after high risk surgeries (mastectomy, amputation, hysterectomy, cholecystectomy, hernia repair, thoracotomy, thyroidectomy, and knee/hip arthroplasty), and to evaluate its impact on quality of life and recovery.

Methods

The Institutional Review Board of the Centro Hospitalar São João approved the study protocol (Centro Hospitalar São João Ethics Committee, Alameda Hernâni Monteiro, 4200-310 Porto, Portugal - Chairperson Prof Filipe Nuno Alves Santos Almeida, Ethical approval number 198-13), and written informed consent was obtained from all patients. This prospective cohort study was carried out in the multidisciplinary Post-Anaesthesia Care Unit (PACU) at the 1124-bed Centro Hospitalar São João, a community teaching hospital in Porto, Portugal. It was conducted in patients scheduled for elective surgery admitted in the PACU from June to August 2013.

Inclusion criteria were all consecutive adult patients undergoing orthopedic (limb amputation, total knee and hip arthroplasty), thoracic (thoracotomy), gynecologic (hysterectomy), and general surgery (mastectomy, thyroidectomy, inguinal hernia repair and cholecystectomy). Patients unable to give informed consent, patients with cognitive impairment (Mini-mental State Examination < 24) and patients submitted to emergent or urgent surgery were excluded.

The following clinical variables were recorded preoperatively (T0): age, sex, body weight, height, body mass index (BMI) and the American Society of Anaesthesiologists physical status (ASA-PS). Additionally, pre-admission comorbidities and history of hypertension, diabetes, hyperlipidaemia, chronic obstructive pulmonary disease (COPD), cerebrovascular disease, psychiatric disease, smoking and benzodiazepines therapy were recorded. Preoperative cognitive function was evaluated with the Mini Mental State Examination.

Intra-operatively, we recorded duration and type of anaesthesia. Analgesic or anxiolytic drugs administered in the 24-hour period after surgery were registered.

Brief Pain Inventory (Appendix 1) was used to assess CPOP. BPI is a widely used questionnaire designed to assess the patient-reported outcome of pain making it a suitable method for detecting chronic pain in those adults who are able to provide information about them. (6, 7)

QoL was evaluated with the EQ-5D EuroQol five-dimension questionnaire (Appendix 2) and QoR after anaesthesia with the 15-item Quality of Recovery score (Appendix file 3). EQ-5D is a generic questionnaire that measures health outcome and was developed at the European level. The Portuguese version of EQ-5D was designed in 1998. (8) The EQ-5D comprises two parts: the EQ-5D self-classifier, a self-reported description of health problems according to a five dimensional classification i.e., mobility, self-care, usual activities, pain/discomfort

and anxiety/depression; the EQ VAS, a self-rated health status using a visual analogue scale (VAS), similar to a thermometer, to record perceptions of participants own current overall health; the scale is graduated from 0 (the worst imaginable health state) to 100 (the best imaginable state). An index (EQ Index), based on the five dimensions and the EQ VAS and ranging from 0 to 100, was also calculated and used to describe the overall QoL of the patients. (9, 10) We categorized patients into two groups considering their answers to EQ-5D: those with no referred problems and those with problems, regardless of their severity. QoR-15 is a short-form version of the 40-question original questionnaire and provides a valid, reliable, responsive, easy-to-use, extensive, and efficient method of evaluating the quality of postoperative recovery. It may be used to assess the impact of changes in health care delivery for quality assurance purposes. (5) We performed QoR-15 before surgery (T0) and 24 hours after surgery (T24).

Quality of life and BPI evaluations were performed preoperatively (T0) and 3 months after surgery (T3) in 175 patients. The primary endpoint was CPOP. Each patient admitted was evaluated prospectively for the diagnosis of CPOP using BPI conducted by research staff physicians. All patients yielding a positive BPI at 3 months post-operatively were considered to have CPOP.

Results

Admission and pre-admission patient characteristics (T0)

175 patients were enrolled in this study (Table 2), 62 (35%) were male and 113 (65%) were female. The median age was 62 years old and 140 (80%) patients were considered ASA-PS I/II and 35 (20%) ASA-PS III/IV. The median BMI was 26 kg/m^2. 84 (48%) patients had history of hypertension, 61 (31%) of dyslipidaemia, 11 (6%) of COPD, 34 (19%) of diabetes, 10 (6%) of cerebrovascular disease, and 24 (14%) of psychiatric disease. 24 (14%) patients were smokers. 42 (24%) patients confirmed taking benzodiazepines daily as usual medication.

Concerning type of surgery, 26 (15%) patients underwent thyroidectomy, 14 (8%) thoracotomy, 13 (7%) amputation, 25 (15%) cholecystectomy, 29 (17%) inguinal hernia repair, 12 (7%) hysterectomy, 37 (21%) mastectomy, and 19 (11%) orthopaedic surgery. Type of surgery was not associated with CPOP at 3 months (p=0.090) (Table 3).

35 (20%) patients reported pain before surgery. Patients with CPOP at T3, had more frequently "pain before surgery" (p<0.001) and were less frequently on "benzodiazepines therapy" (p=0.015).

At T0, the problems reported by patients with CPOP were significantly larger in all EQ-5D dimensions: "mobility" (p=0.024), "self-care" (p=0.001), "usual activities" (p<0.001), and "pain/discomfort" (p<0.001), but "anxiety/depression" (p=0.797). Patients with CPOP reported lower median EuroQol Visual analogue scale (EQ VAS) (65 vs. 80, p<0,001), and lower VAS index (64 vs. 91, p<0,001) (Table 4).

Concerning QoR-15 scores, CPOP patients presented with lower total median scores at T0 in the following domains: "getting support from hospital doctors and nurses" (10 vs. 10, p=0.016), "able to return to work or usual home activities" (10 vs. 10, p=0.026), "moderate pain" (9 vs. 10, p<0.001), "severe pain" (10 vs. 10, p<0.001) and for a "global score" (125 vs. 132, p=0.021) (Table 5).

During surgery and PACU stay results

Regarding anaesthesia, 146 (83%) patients received general or combined general-locorregional anaesthesia while 29 (17%) received locorregional anaesthesia. The median duration of the anaesthesia was 120 minutes and median PACU stay was 90 minutes. The median value for pain at PACU admission and discharge using VAS was 0 (Table 6).

24h post-operatively (T24) results

At T24, 81 (46%) patients reported pain. Pain 24 hours after surgery was associated with more CPOP at 3 months follow-up (p=0.021). QoR-15 mean global score was lower for CPOP patients (103 vs. 121, p<0.001). At T24, when evaluating each domain of QoR-15, CPOP patients have lower scores at “been able to enjoy food” (5 vs. 9, p=0.022), “feeling rested” (7 vs. 9, p=0.001), “moderate pain” (5 vs. 7, p=0.004), “severe pain” (10 vs. 10, p=0.009), “nausea or vomiting” (10 vs. 10, p=0.049), and “feeling sad or depressed”(8 vs. 10, p=0.013) (Table 5).

3 months post-operatively (T3) results

49 (28%) patients had CPOP 3 months after surgery. Patients with CPOP at 3 months follow-up had more frequently pain 24 hours after surgery (p=0.021). Moreover, half of our patients with positive BPI before surgery still had pain at T3.

At this time, the problems reported by patients with CPOP were significantly larger in all EQ-5D dimensions: “mobility” (p=0.001), “self-care” (p=0.001), “usual activities” (p<0.001), “pain/discomfort” (p<0.001), and “anxiety/depression” (p=0.002). Patients with CPOP reported lower median EuroQol Visual analogue scale (EQ VAS) (60 vs. 87, p<0,001) as well as lower VAS index (64 vs. 91, p<0,001) (Table 4).

Discussion

Our study reports that 3 months after surgery 28% of patients had CPOP. This incidence, similar to those of the previous studies, may be viewed as an important indicator regarding the economic burden and the significant impact on quality of life.

In our study, a considerable number of patients, all well characterized according to their medical history, were submitted to various types of surgeries, different kinds of anaesthetic management and diverse times of recovery. The population was extensively evaluated by several parameters that are known to influence the quality of recovery and it was possible to determine its impact on quality of life. According to our knowledge, this is also the first study recording the incidence of chronic postoperative pain after thyroidectomy.

Regarding risk factors and predictors of CPOP, previous studies reported that age (11) and gender (12, 13) are non-modifiable patient-related risk factors: younger patients and female patients tend to have a higher risk of developing CPOP than older patients and male patients. However, in our study we did not find any difference according to age or gender. Regarding modifiable risk factors, previous studies found that high body mass index (≥25) (11), severe preoperative pain (13-15), higher incidence of postoperative complications (16), and the presence of chronic pain in other areas of the body (17) were also considered to be risk factors. Although in the present study, we could not find that a higher BMI and the presence of chronic pain in other areas of the body were associated with an increase in CPOP incidence, we could find that CPOP was related with severe postoperative pain as reported in many previous studies (2, 3), which corroborates the thesis that CPOP may be associated with severe and/or poorly controlled acute pain after surgery. Thus, we may theorize that aggressive acute pain management may diminish the development of CPOP. (2, 3) Moreover, certain psychological factors including anxiety, depression, posttraumatic stress disorder, past life traumas (18), catastrophizing (19), and stress and duration of disability (time to return from work) (20) were associated with CPOP in various studies. We did not perform a psychological evaluation of our patients by a specialized therapist; nonetheless we enquired patients about the presence of any psychiatric disorder and psychiatric medication use. We observed that those taking benzodiazepines daily had less frequently CPOP at 3 months after surgery, which is in accordance to previous studies (21) regarding psychological status of patients. In a particularly anxious patient, pre-existing pain may be intensified by fear and anxiety, and benzodiazepines may reduce the amount of intraoperative anaesthetic and postoperative analgesic needs. (21) During the intraoperative and postoperative

periods, important surgical factors include: the type of surgery (22), anatomical location of surgery, surgical technique (23), and the extent of nerve injury and tissue ischemia (23). (3) Some surgeries are associated with higher incidence of CPOP, such as mastectomy, thoracotomy and inguinal hernia repair.

In addition, we did not find differences in CPOP incidence between the different types of surgeries, but we must recognise that the limited number of patients and the relatively high number of surgeries' groups may have limited any conclusion.

Type of anaesthesia has been implicated on the development of CPOP but in the present study we did not find any difference according to this variable, which is consistent with previous results. (24)

Although several risk factors have been implicated in the development of this pain condition, no single factor appears to dominate. It is believed that less than 20% of the overall risk can be predicted by the severity of postoperative pain. (25) Yet, it might be possible that the cumulative risk is crucial in patients with multiple risk factors. Whenever possible, identifying and aggressively treating the underlying cause of nervous tissue injury is essential. This may explain why half of our patients with positive BPI before surgery still had pain at T3. Surgery on a painful body area did not treat the pain, which should point us towards an alternate cause.

Patients who presented CPOP after surgery included those with pre-existing pain (positive BPI before surgery) and those with newly developed pain. Before surgery, patients who later reported CPOP presented significantly more problems in all EQ-5D dimensions except "anxiety/depression". At T3, patients with CPOP reported significantly more problems in all EQ-5D dimensions. Before and after surgery, these patients also reported lower mean EQ VAS. All mentioned results show a clear relationship between CPOP and poor own perception of health related-QoL.

When evaluating each domain of QoR-15 at T24, CPOP patients had lower scores at "been able to enjoy food", "feeling rested", "moderate pain", "severe pain", "nausea or vomiting", and "feeling sad or depressed".

We propose that some of the baseline values obtained preoperatively may be underestimated providing many patients were possibly anxious, medically unstable or in pain before surgery. However, we should not ignore that CPOP patients already felt more pain, moderate and severe, before surgery when compared with those without CPOP at T3. This may also explain why some patients develop pain and others do not, leading us to believe certain patients have a higher risk for developing CPOP. It is essential to have means to discriminate between these two groups in

order to find strategies to prevent CPOP. Although we believe prevention is the key, its effect is often small and the evidence is not consistent. Currently, there is almost nothing suggesting a reliable and effective method for prevention is possible. Nonetheless, as previous mentioned, the severity of postoperative pain has been recognized as a predicting factor for chronic pain in many studies. We have excellent techniques aimed at this and it may be that focusing more attention on patients in severe pain after surgery will be of benefit. (2) Future studies concentrating on the effect of aggressive management of acute postoperative pain on long-term CPOP are crucial.

Additionally, previous studies reported that QoR-15 was able to discriminate between men and women (26, 27) and it has already been found a negative association between QoR-15 and duration of surgery and duration of time spent in PACU. However, in our study, no relation has been found between QoR-15 score and patient age (28, 29), possibly explained by the fact that older people tend to report less pain, nausea and vomiting and scoring their recovery more positively. (5) Despite this, our study shows a clear relation between a worse recovery and the development of CPOP. Not only did CPOP patients felt more pain, moderate or severe, before and after surgery compared to those who were CPOP-negative at T3, but they also experienced incapacity to appreciate food and to feel rested, nausea and vomiting, and felt sad or depressed, immediately after surgery. All these in addition to an overall worse QoR-rate both at T0 and T24 suggest these patients have poorer quality of recovery and consequently lower quality of life.

This study has several limitations that must be addressed. We did not exclude patients with pain before surgery and that may be a confounding factor. The sample was not homogenous since we included adult patients with a variety of surgeries. In this study the anaesthetic management was not standardized: there was no anaesthetic protocol to follow and the postoperative management was not guided by any protocol. We also had a small patient population and we studied patients submitted to wide variety of surgeries and this may have increased statistical type II error. Even so, the sample may have been very small to detect other statistically significant factors. Moreover, we did not study some variables known to be associated with CPOP like the nature, intensity, and duration of pre-surgical pain.

In conclusion, CPOP is an increasingly prevalent healthcare problem associated with significant morbidity and it represents an important outcome measure after surgery. In our study its incidence was relevant (28%) and patients

with CPOP reported worse QoR at T24 using QoR-15, and worse QoL 3 months after surgery with EQ-5D than those without CPOP.

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Tables and Figures

Figure 1 - Risk factors for the development of CPOP.

As illustrated by McGreevy et al. (3)

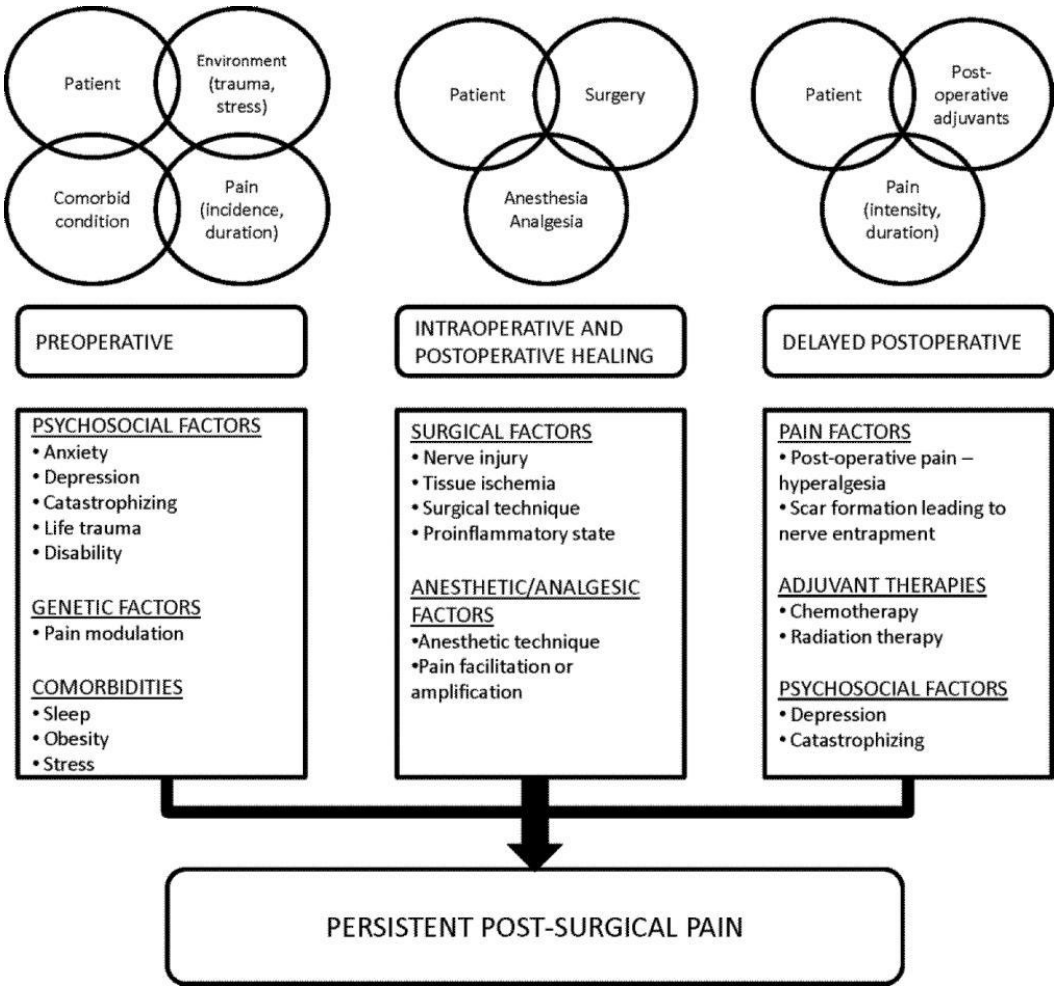


Table 1 – Prevalence of CPOP according to type of surgery (2, 3, 30, 31).

	Prevalence of CPOP
Mastectomy	20–50%
Amputation	30–85%
Hysterectomy	5–32%
Hernia repair	5–35%
Thoracotomy	5–65%
Thyroidectomy	*unknown*
Total knee arthroplasty	19-30%
Total hip arthroplasty	28-41%
Cholecystectomy	26%

Table 2 – Pre-admission patient characteristics.

	All patients (n=175)	**No CPOP at T3 (n=126/72%)**	**CPOP at T3 (n=49/28%)**	**p**
Age (years), median	62 (48-70)	61 (46-69)	63 (53-72)	0.207
Gender, n (%)				0.125
• Male	62 (35)	49 (39)	13 (27)	
• Female	113 (65)	77 (61)	36 (74)	
ASA, n (%)				0.449
• I/II	140 (80)	99 (79)	41 (84)	
• III/IV	35 (20)	27 (21)	8 (16)	
BMI (kg/m2), median	26 (23-30)	26 (23-30)	26 (23-28)	0.543
Hypertension, n (%)	84 (48)	62 (49)	22 (45)	0.608
Dyslipidaemia, n (%)	61 (31)	46 (37)	15 (31)	0.462
Cerebrovascular disease, n (%)	10 (6)	7 (6)	3 (6)	0.567
Diabetes, n (%)	34 (19)	27 (21)	7 (14)	0.284
COPD, n (%)	11 (6)	7 (6)	4 (8)	0.370
Smoking, n (%)	24 (14)	17 (14)	7 (14)	0.891
Psychiatric disease, n (%)	24 (14)	14 (11)	10 (20)	0.108
Benzodiazepines therapy, n (%)	**42 (24)**	**24 (19)**	**18 (37)**	**0.015**
Pain before surgery, n (%)	**35 (20)**	**17 (14)**	**18 (37)**	**<0.001**

Table 3 – CPOP incidence according to the type of surgery.

	All patients (n=175)	**No CPOP at T3 (n=126/72%)**	**CPOP at T3 (n=49/28%)**	**p**
Type of surgery, n (%)				0.090
• Thyroidectomy	26 (15)	20 (16)	6 (12)	
• Thoracotomy	14 (8)	11 (9)	3 (6)	
• Amputation	13 (7)	9 (7)	4 (8)	
• Cholecystectomy	25 (14)	23 (18)	2 (4)	
• Hernia repair	29 (17)	21 (17)	8 (16)	
• Hysterectomy	12 (7)	9 (7)	3 (6)	
• Mastectomy	37 (21)	24 (19)	13 (27)	
• Hip/Knee arthroplasty	19 (11)	9 (7)	10 (20)	

Table 4 – EQ-5D results.

	All patients (n=175)	No CPOP at T3 (n=126/72%)	CPOP at T3 (n=49/28%)	P
Before surgery (To), n (%)				
Mobility	**119 (68)**	**91 (74)**	**28 (58)**	**0.024**
Self-care	**142 (81)**	**108 (88)**	**34 (71)**	**0.001**
Usual activities	**126 (72)**	**97 (79)**	**29 (60)**	**<0.001**
Pain/Discomfort	**105 (60)**	**85 (69)**	**20 (42)**	**<0.001**
Anxiety/Depression	55 (31)	42 (34)	13 (27)	0.797
VAS	**75 (50-85)**	**80 (50-90)**	**65 (46-80)**	**0.039**
VAS index	**91 (64-100)**	**91 (81-100)**	**64 (50-81)**	**<0.001**
After surgery (T3), n (%)				
Mobility	**123 (70)**	**99 (79)**	**24 (49)**	**0.001**
Self-care	**131 (75)**	**105 (83)**	**26 (53)**	**0.001**
Usual activities	**115 (66)**	**100 (79)**	**15 (31)**	**<0.001**
Pain/Discomfort	**108 (62)**	**101 (80)**	**7 (14)**	**<0.001**
Anxiety/Depression	**98 (56)**	**80 (64)**	**18 (37)**	**0.002**
VAS	**80 (60-90)**	**87 (70-95)**	**60 (50-80)**	**<0.001**
VAS index	**91 (64-100)**	**91 (81-100)**	**64 (50-81)**	**<0.001**

Table 5 – QoR-15 results

	All patients (n=175)	**No CPOP at T3 (n=126)**	**CPOP at T3 (n=49)**	**P**
Before surgery (T0)				
1. Able to breathe easy	10 (10-10)	10 (10-10)	10 (10-10)	0.876
2. Been able to enjoy food	10 (10-10)	10 (10-10)	10 (8-10)	0.072
3. Feeling rested	9 (5-10)	8 (5-10)	9 (5-10)	0.684
4. Have had a good sleep	9 (5-10)	9 (5-10)	7 (4-10)	0.401
5. Able to look after personal toilet and hygiene unaided	10 (10-10)	10 (10-10)	10 (10-10)	0.239
6. Able to communicate with family or friends	10 (10-10)	10 (10-10)	10 (10-10)	0.687
7. Getting support from hospital doctors and nurses	**10 (10-10)**	**10 (10-10)**	**10 (10-10)**	**0.016**
8. Able to return to work or usual home activities	**10 (8-10)**	**10 (9-10)**	**10 (6-10)**	**0.026**
9. Feeling comfortable and in control	10 (7-10)	10 (8-10)	10 (5-10)	0.097
10. Having a feeling of general well-being	9 (6-10)	9 (7-10)	8 (5-10)	0.105
11. Moderate pain	**10 (8-10)**	**10 (10-10)**	**9 (4-10)**	**<0.001**
12. Severe pain	**10 (10-10)**	**10 (10-10)**	**10 (8-10)**	**<0.001**
13. Nausea or vomiting	10 (10-10)	10 (10-10)	10 (10-10)	0.177
14. Feeling worried or anxious	5 (3-9)	5 (2-9)	5 (3-9)	0.997
15. Feeling sad or depressed	8 (5-10)	9 (5-10)	7 (4-10)	0.107
Total	**131 (114-140)**	**132 (119-142)**	**125 (99-138)**	**0.021**
24h after surgery (T24)				
1. Able to breathe easy	10 (8-10)	10 (9-10)	10 (7-10)	0.094
2. Been able to enjoy food	**8 (4-10)**	**9 (5-10)**	**5 (1-10)**	**0.022**
3. Feeling rested	**8 (6-10)**	**9 (7-10)**	**7 (5-8)**	**0.001**
4. Have had a good sleep	7 (4-9)	8 (5-10)	7 (2-9)	0.366
5. Able to look after personal toilet and hygiene unaided	8 (2-10)	9 (2-10)	7 (2-10)	0.265
6. Able to communicate with family or friends	10 (9-10)	10 (9-10)	10 (7-10)	0.144
7. Getting support from hospital doctors and nurses	10 (9-10)	10 (9-10)	10 (9-10)	0.973
8. Able to return to work or usual home activities	6 (2-9)	7 (3-9)	5 (1-9)	0.246
9. Feeling comfortable and in control	9 (6-10)	9 (7-10)	8 (5-10)	0.165
10. Having a feeling of general well-being	8 (5-10)	8 (6-10)	7 (5-9)	0.096
11. Moderate pain	**5 (3-10)**	**7 (4-10)**	**5 (3-6)**	**0.004**
12. Severe pain	**10 (9-10)**	**10 (10-10)**	**10 (7-10)**	**0.009**
13. Nausea or vomiting	**10 (8-10)**	**10 (10-10)**	**10 (6-10)**	**0.049**
14. Feeling worried or anxious	8 (5-10)	8 (5-10)	8 (3-10)	0.506
15. Feeling sad or depressed	**10 (6-10)**	**10 (8-10)**	**8 (5-10)**	**0.013**
Total	**115 (98-128)**	**121 (104-133)**	**103 (83-118)**	**<0.001**

Table 6 – During surgery and at PACU stay results.

	All patients (n=175)	**No CPOP at T3 (n=126)**	**CPOP at T3 (n=49)**	**P**
Anaesthesia duration (min), median	120	120	120	0.107
Type of anaesthesia, n (%)				0.149
• General/Combined general-locorregional	146 (83)	109 (86)	37 (75)	
• Locorregional	29 (17)	17 (14)	12 (25)	
PACU stay duration (min), median	90 (70-120)	90 (66-115)	95 (75-128)	0.470
VAS for pain at PACU admission	0 (0-5)	0 (0-5)	1 (0-5)	0.411
VAS for pain at PACU discharge	0 (0-2)	0 (0-2)	0 (0-2)	0.897

Appendix 1 – Brief Pain Inventory (BPI)

STUDY ID# _____ HOSPITAL # _____

DO NOT WRITE ABOVE THIS LINE

Brief Pain Inventory (Short Form)

Date: _____/_____/_____ Time: _____

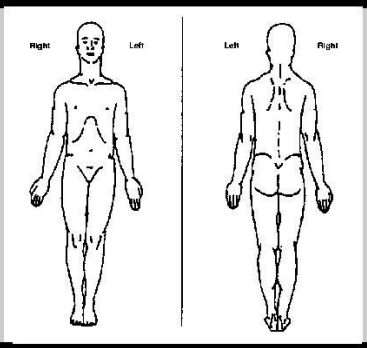
Name: _____ _____ _____

Last First Middle Initial

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these every-day kinds of pain today?

   1. Yes 2. No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its worst in the last 24 hours.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

4. Please rate your pain by circling the one nuimber that best describes your pain at its least in the last 24 hours.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

5. Please rate your pain by circling the one number that best describes your pain on the average.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

6. Please rate your pain by circling the one number that tells how much pain you have right now.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

7. What treatments or medications are you receiving for your pain?

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
No Relief										Complete Relief

9. Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

B. Mood

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

C. Walking Ability

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

D. Normal Work (includes both work outside the home and housework)

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

E. Relations with other people

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

F. Sleep

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

G. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

Appendix 2 – EQ-5D: EuroQol five-dimension questionnaire

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

- I have no problems in walking about ❑
- I have slight problems in walking about ❑
- I have moderate problems in walking about ❑
- I have severe problems in walking about ❑
- I am unable to walk about ❑

SELF-CARE

- I have no problems washing or dressing myself ❑
- I have slight problems washing or dressing myself ❑
- I have moderate problems washing or dressing myself ❑
- I have severe problems washing or dressing myself ❑
- I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

- I have no problems doing my usual activities ❑
- I have slight problems doing my usual activities ❑
- I have moderate problems doing my usual activities ❑
- I have severe problems doing my usual activities ❑
- I am unable to do my usual activities ❑

PAIN / DISCOMFORT

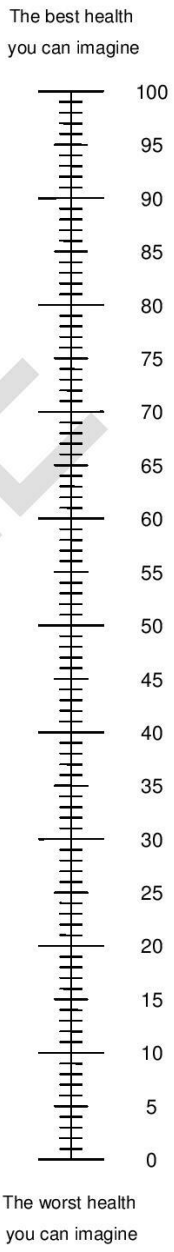
- I have no pain or discomfort ❑
- I have slight pain or discomfort ❑
- I have moderate pain or discomfort ❑
- I have severe pain or discomfort ❑
- I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

- I am not anxious or depressed ❑
- I am slightly anxious or depressed ❑
- I am moderately anxious or depressed ❑
- I am severely anxious or depressed ❑
- I am extremely anxious or depressed ❑

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY =



Appendix 3 – QoR-15: 15-item Quality of Recovery score

Date: _ _ / _ _ / _ _ Study #: _____

Preoperative ☐ Postoperative ☐

PART A

How have you been feeling in the last 24 hours?

(0 to 10, where: 0 = none of the time [poor] and 10 = all of the time [excellent])

1.	Able to breathe easily	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
2.	Been able to enjoy food	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
3.	Feeling rested	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
4.	Have had a good sleep	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
5.	Able to look after personal toilet and hygiene unaided	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
6.	Able to communicate with family or friends	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
7.	Getting support from hospital doctors and nurses	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
8.	Able to return to work or usual home activities	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
9.	Feeling comfortable and in control	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time
10.	Having a feeling of general well-being	None of the time	0	1	2	3	4	5	6	7	8	9	10	All of the time

PART B

Have you had any of the following in the last 24 hours?

(10 to 0, where: 10 = none of the time [excellent] and 0 = all of the time [poor])

11.	Moderate pain	None of the time	10	9	8	7	6	5	4	3	2	1	0	All of the time
12.	Severe pain	None of the time	10	9	8	7	6	5	4	3	2	1	0	All of the time
13.	Nausea or vomiting	None of the time	10	9	8	7	6	5	4	3	2	1	0	All of the time
14.	Feeling worried or anxious	None of the time	10	9	8	7	6	5	4	3	2	1	0	All of the time
15.	Feeling sad or depressed	None of the time	10	9	8	7	6	5	4	3	2	1	0	All of the time

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and those listed at: http://www.who.int/ictrp/network/primary/en/index.html

Maximum length of reports of randomised controlled trials is 3500 words. Please provide a structured abstract (300 words, see subheading Structured Abstract).

Observational Study (Cohort, Case-control, Cross-sectional, Case Series)
Authors are requested to report these in accordance with the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) statement [www.strobe-statement.org].

Maximum length of reports of observational studies is 3500 words. Please provide a structured abstract (300 words, see subheading Structured Abstract).

Studies of Diagnostic Accuracy

Authors are requested to report these in accordance with STARD (STandard for the Reporting of Diagnostic accuracy) statement [www.stard-statement.org].

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Systematic Reviews (with or without meta-analysis)

Authors are requested to submit these as 'Original articles' (not 'Reviews') and report them in accordance with the PRISMA (Transparent Reporting of Systematic Reviews and Meta-Analyses) Statement [www.prisma-statement.org]. This ensures that enough information is provided for editors, peer reviewers, and readers to see how the study was performed and to judge whether the findings are likely to be reliable (see EJA Editorial: Adherence to guidelines for improved quality of data reporting: where are we today?). Please provide the following:

• A flow chart showing the progress of retrieved reports through the review
• A checklist for editors and reviewers (not for publication) showing that you have described the recommended respective key points in your report.

Maximum length of reports of systematic reviews is 3500 words. Please provide a structured abstract (300 Words, see subheading Structured Abstract). Authors are encouraged to publish additional material (for instance, large tables, figures with forest

plots, data from subgroup analyses etc.) as Supplemental Digital Content (see above for details).

Conventional, Non-systematic Reviews

These are usually commissioned. Maximum length of reviews is 3500 words. Please provide an unstructured abstract (max. 250 words). Please include a title page giving the author's name, address, email address, phone and fax numbers, as well as an Acknowledgement statement (see paragraph: Acknowledgements) and signed copyright forms.

Practice Guidelines

In general, published statements intended to guide clinical care (e.g., Guidelines, Practice Parameters, Recommendations, Consensus Statements, Position Papers) should describe:

1. The clinical problem to be addressed;
2. The mechanism by which the statement was generated;
3. A review of the evidence for the statement (if available), and;
4. The statement on practice itself.

As more than one group or society may issue statements on the same topic, this often results in confusion amongst clinicians. To minimize confusion and to enhance transparency, such statements should begin with the following bulleted phrases, followed by brief comments addressing each phrase:

- What other guideline statements are available on this topic?
- Why was this guideline developed?
- How does this statement differ from existing guidelines?
- Why does this statement differ from existing guidelines?

Editorials

Editorials discuss issues that are not directly related to published material. Editorials are usually commissioned. Editorials should be up to 1500 words long with no more than 15 references. Please include a title page giving all authors' names, addresses, email addresses, phone and fax numbers, as well as an Acknowledgement statement

(see paragraph: Acknowledgements) and signed copyright forms. Editorials do not have an abstract.

Commentaries

Commentaries discuss issues that are directly related to published material. Commentaries accompany original articles, critically appraise their results and put their conclusions into a wider context. Commentaries are always commissioned and should be up to 1000 words long with no more than 10 references. Commentaries do not have an abstract. Please include a title page giving the author's name, address, email address, phone and fax numbers, as well as an Acknowledgement statement (see paragraph: Acknowledgements) and signed copyright forms.

Correspondence

In this section, we publish case reports, letters and replies. Items in the Correspondence section are peer reviewed. Please look at a very recent copy of the European Journal of Anaesthesiology to see how the material should be presented. The format (layout) for the Correspondence section is quite different from our other articles. The absolute maximum is 1000 words, which must include the space for any tables and illustrations (this is approximately two sides of printed matter in the Journal). There should be no more than 4 authors, if more than 4 are stated then a letter justifying the number of authors and listing what each contributed should be submitted with the article. References are limited to seven.

Correspondence articles do not have an abstract. Please include a title page giving the author's name, address, email address, phone and fax numbers, as well as an Acknowledgement statement (see paragraph: Acknowledgements) and signed copyright forms.

Case Reports

Case reports should follow the guidance for correspondence (see above). In addition case reports dealing with patients must state that informed consent to publication was obtained from the patient or guardian (or was granted by a competent ethics committee).

Presentation of papers

Title Page

The Title Page should carry the full title of the paper and a short title to be used as a 'running head' (and which should be so identified). Please, include the study design in the title; for instance, "randomised controlled trial", or "systematic review". Titles should be as informative and complete as possible. The EJA Editorial:How to write a good title provides some help. The first name, middle initial and last name of each author and their affiliations should appear. Academic degrees should not be stated. If the work is to be attributed to a department or institution, its full name should be included. The name and address of the corresponding author and the name and address of the author to whom requests for reprints should be made should also appear on the Title Page.

Structured Abstract

For original articles, the second page should carry an abstract, which will be printed at the beginning of the paper and should not be more than 300 words. Use the following headings and information as appropriate (which are adapted from the BMJ and JAMA websites). The abstract should be usable as it stands by abstracting journals. Because of this it should contain some numerical data (if appropriate), not just statistical statements, and it should not contain abbreviations or references (see EJA Editorial: Writing the abstract: completeness and accuracy matter).

Example: Randomised controlled trial, observational study, diagnostic study, animal study

Background: Explaining the clinical (or other) importance of the study question.

Objective(s): Including a clear statement of the main aim(s) of the study and the major hypothesis tested or research question posed. Avoid statements such as "We aimed to evaluate the effectiveness of X".

Design: For example, randomised controlled study, case control study, crossover study, observational study, survey, diagnostic test etc.

Setting: Include the level of care e.g. primary, secondary; number of participating centres. Be general rather than give the name of the specific centre, but give the geographical location if this is important. Include the dates of the study period.

Patients, other participants (delete what does not apply): Numbers entering and completing the study, sex, and ethnic group if appropriate. Give clear definitions of how selected, entry and exclusion criteria. For animal studies, this information should be included in the Design or Setting section.

Intervention(s): What, how, when and for how long. This heading can be deleted if there were no interventions but should normally be included for randomised controlled trials, cross over trials, and before and after studies.

Main outcome measures: What was the primary endpoint? What outcome measures were planned in protocol, which were finally measured (if different, explain why)?

Results: Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance.

Conclusions: Primary conclusions and their implications, suggest areas for further research if appropriate.

Trial registration: The trial registration number and the name of the registry must be stated at the end of the abstract, for example: "Trial registration:Clinicaltrials.gov identifier: NCT00405977."

Example: Systematic reviews with or without meta-analyses

Background:

Objective(s):

Design: For example: Systematic review of randomised controlled trials with meta-analyses.

Data sources: Where included studies were retrieved from? Include years searched.

Eligibility criteria: Describe inclusion and non-inclusion criteria of selected studies.

Results:

Conclusions:

Text

The remainder of the text should be divided into sections headed Introduction, Methods (including ethical and statistical information), Results, and Discussion (including a conclusion).

Acknowledgements

The acknowledgements section should be headed 'Acknowledgements relating to this article' and contain four distinct statements in three separate paragraphs:

1. Assistance with the article. Acknowledgements should be made only to those who have made a substantial contribution to the study. Authors are responsible for obtaining written permission from people acknowledged by name in case readers infer their endorsement of data and conclusions. If there was no assistance state: none declared.

2. Financial support and sponsorship. You must make reference to all relevant sources of funding concerning this article. If there were no sources of funding please state: none declared.

3. Conflicts of interest. You must make reference to all relevant conflicts of interest concerning this article. If there are no conflicts of interest please state: none declared.

4. Presentation. Presentations of preliminary data at, for example, international meetings should be acknowledged separately. If preliminary data was not previously presented please state: none declared.

For example:

Acknowledgements relating to this article

Assistance with the study: We would like to thank Dr John A. Smith for his assistance with the study.

Financial support and sponsorship: This work was supported by the Department of Anaesthesiology, London Hospital, London, UK.

Conflicts of interest: A has received honoraria from Company Z. B is currently receiving a grant (#12345) from Organisation Y, and C is on the speaker's bureau for Organisation X. For the remaining authors none were declared.

Presentation: Preliminary data for this study were presented as a poster presentation at the European Society of Anaesthesiology (ESA) Euroanaesthesia, 9–12 June 2012, Paris.

References

Number references consecutively in the order in which they are first mentioned in the text. Identify references in the text, tables and legends using superscripted Arabic numerals that are placed after the punctuation. References cited only in tables or in legends to figures should be numbered in accordance with the sequence established by the first identification in the text of the particular table or illustration.

Use the Vancouver reference system as adopted by the U.S. National Library of Medicine ensuring that all journal titles conform to Index Medicus approved abbreviations. If in doubt, look up the reference list of a recent paper published in the *European Journal of Anaesthesiology*.

Avoid citing abstracts unless from a MEDLINE or EMBASE indexed journal. Unpublished observations and personal communications should not be used as references, although references to written (not verbal) communications may be inserted (in parentheses) in the text. Manuscripts that have been accepted but not yet published (e.g. Epub ahead of print) should be included in the list, followed by (in press). Information from manuscripts not yet accepted may be cited only in the text as (unpublished observations). Authors should verify references against the original documents before submitting the article.

Electronic or online references should be cited in the reference list only if the material referenced is a specific article (e.g. a paper published in a web-based journal); see below for correct style. Less specific references (e.g. the web pages of societies, organisations and university departments) should not appear in the references; instead the URL should be cited in full in the text.

Authors must confirm that the details of these references are accurate and complete. In the full list of references give the names and initials of all authors. If there are more than six, cite only the first three names followed by et al. The authors' names are followed by the title of the article: the title of the journal (italics) abbreviated according

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Journal articles

Pollard BJ, Bryan A, Bennett D et al. Recovery after oral surgery with halothane, enflurane, isoflurane or propofol anaesthesia. *Br J Anaesth* 1994; **72**: 559–566.

Books

Korttila K. Recovery period and discharge. In: White P, ed. *Outpatient Anaesthesia*. New York, USA: Churchill Livingstone Inc, 1990: 369–395.

Chapter in a book:

Pessayre D, Feldmann G, Haouzi D, Fau D, Moreau A, Neumann M. Hepatocyte apoptosis triggered by natural substances (cytokines, other endogenous molecules and foreign toxins). In Cameron RG, Feuer G (editors): *Apoptosis and its Modulation by Drugs. Handbook of Experimental Pharmacology*. Berlin: Springer-Verlag; 2000, pp. 59-108.

Electronic articles:

Margolis PA, Stevens R, Bordley WC, Stuart J. From concept to application: the impact of a community-wide intervention to improve the delivery of preventive services to children. Pediatrics [online serial] 2001; 108:e42. http://www.pediatrics.org/cgi/content/full/108/3/e42. [Accessed 20 September 2001].

Tables

References to tables should be made in order of appearance in the text and should be in Arabic numerals in parentheses, e.g. (Table 1). Each table should be typed on a separate sheet in 1.5 spacing. Tables should not be submitted as photographs. Each table should have a brief title as a heading. Vertical rules should not be used. Place explanatory matter in footnotes, not in the heading. Authors are discouraged from using abbreviations in tables. If abbreviations are necessary then please explain them in the

table's footnotes. Identify statistical measures of variations, such as standard deviation (SD) and standard error of the mean (SEM).

Be sure that each table is cited in the text. If you use data from another published or unpublished source, obtain permission and acknowledge the source fully.

Authors are encouraged to submit non-essential tables as supplemental digital content for publication online only. See Supplemental Digital Content section for more details.

Figures

A) Creating Digital Artwork

1. Learn about the publication requirements for Digital Artwork: http://links.lww.com/ES/A42

2. Create, Scan and Save your artwork and compare your final figure to the Digital Artwork Guideline Checklist (below).

3. Upload each figure to Editorial Manager in conjunction with your manuscript text and tables.

B) Digital Artwork Guideline Checklist

Here are the basics to have in place before submitting your digital artwork:

- Artwork should be saved as TIFF, EPS, or MS Office (DOC, PPT, XLS) files. High resolution PDF files are also acceptable.
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- Photographs and radiographs with text must be saved as postscript or at a resolution of at least 600 dpi.
- Each figure must be saved and submitted as a separate file. Figures should not be embedded in the manuscript text file.

Remember:

- References to figures should be made in order of appearance in the text and should be in Arabic numerals in parentheses, e.g. (Fig. 2).
- Number figures in the figure legend in the order in which they are discussed.
- Upload figures consecutively to the Editorial Manager web site and enter figure numbers consecutively in the Description field when uploading the files.
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Captions should be typed in 1.5 spacing, beginning on a separate page. Each figure should be assigned an Arabic numeral, e.g. (Figure 3) and a brief title as a heading. Internal scales should be explained and staining methods for photomicrographs should be identified.

Units of measurement

Scientific measurements should be given in SI units. Blood pressure, however, may be expressed in mmHg and haemoglobin as g dL-1.

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Authors are discouraged from using abbreviations. If an abbreviation is necessary please use only standard abbreviations. Avoid abbreviations in the title and abstract.

The full term for which an abbreviation stands should precede its first use in the text unless it is a standard unit of measurement.

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Authors may submit supplemental digital content (SDC) to enhance their article's text and to be considered for online-only posting. SDC may include the following types of content: text documents, graphs, tables, figures, graphics, illustrations, audio, and video. On the Attach Files page of the submission process, please select Supplemental Audio, Video, or Data for your uploaded file as the Submission Item. If an article with SDC is accepted, our production staff will create a URL with the SDC file. The URL will be placed in the call-out within the article. SDC files are not copy-edited by LWW staff, they will be presented digitally as submitted. For a list of all available file types and detailed instructions, please visit http://links.lww.com/A142.

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We performed many tests on the degrees of flexibility in the elbow (see Video, Supplemental Digital Content 1, which demonstrates elbow flexibility) and found our results inconclusive.

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